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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/021,403	12/12/2001	Robert J. Schwartz	108328.00031	3652

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EXAMINER	
HAMA, JOANNE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 08/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/021,403	SCHWARTZ ET AL.	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-13,76,80-88,137 and 138* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-13,76,80-88,137 and 138* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 25, 2005, has been entered.

Claims 4 and 79 have been cancelled. Claims 1, 5, 8, 9, 10, 11, 76, 80, 83, 54, 85, and 86 have been amended.

Claims 1, 5-13, 76, 80-88, 137, 138 are pending.

It is noted that the Applicant had indicated that the status of claims 137 and 138 was "new." However, claims 137 and 138 were presented in the Applicant's response, December 7, 2004, and should have been indicated in the Applicant's response, May 25, 2005, as "previously presented."

Information Disclosure Statement

The IDS filed by Applicant May 25, 2005 has been considered. Patent 5,134,210, reference 10 on the IDS has not been considered as the patent is not by Boyd et al.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-13, 76, 80-88, 137, 138 remain rejected in modified form under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

a method of improving or enhancing growth in an offspring from a female pig or rat comprising

introducing an effective amount of a vector into muscle cells by intramuscular injection of the female pig or rat prior to or during gestation of the offspring, wherein the vector is comprised of a nucleic acid sequence encoding SEQ ID NO. 1 or SEQ ID NO. 8, wherein the nucleic acid sequence is operably linked to a hGH3' untranslated region, wherein said nucleotide sequence is expressed in the female and wherein the expression of said nucleotide sequence results in improved or enhanced growth or rate of growth of the offspring, and wherein the vector is not a viral vector.

does not reasonably provide enablement for

a method of improving or enhancing growth in an offspring from a female mammal comprising

introducing an effective amount of a vector into muscle cells of the female mammal prior to or during gestation of the offspring, wherein the vector is capable of expressing any growth hormone releasing hormone or analog thereof in the female mammal during gestation, and wherein the vector comprises a promoter, a nucleotide

sequence capable of expression the GHRH or analog thereof, and a 3' untranslated region, under conditions that promote expression of the nucleotide sequence, and wherein the introduction and expression of the nucleotide sequence results in improved or enhanced growth in said offspring, and wherein the vector is not a viral vector.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for reasons of record, February 25, 2005 and August 5, 2004.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or

unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The claimed invention broadly encompasses any route of delivery of the plasmid DNA (e.g. see claim 8). According to the American History online dictionary, parenteral means: taken into the body or administered in a manner other than through the digestive tract, as by intravenous or intramuscular injection. While the specification teaches that 10mg of plasmid was directly injected into the semitendinous muscle of pigs and that the injected muscle was placed in between a set of calipers and electroporated (Example 7), the specification does not teach that other routes of administration, such as intravenously or intraperitoneally, could be used such that the vector would make its way into muscle, wherein it is expressed.

The claims broadly encompass the use of any "growth hormone releasing hormone or analog thereof" (e.g. see claim 1). The specification teaches that the term "growth hormone releasing hormone" is defined as a hormone which facilitates or stimulates release of growth hormone. Thus, in addition to growth hormone releasing hormone, ghrelin, a hormone that stimulates secretion of growth hormone, would be encompassed by this claim (e.g. see Anderson, et al., 2004, Exp. Biol., Med., 229: 291-302, abstract). However, the specification does not teach administration of ghrelin. No guidance was provided as to whether ghrelin expression resulted in an offspring from a female mammal that has improved or enhanced growth. With regards to "analog," the claimed invention broadly encompasses the use of any GHRH analog and ghrelin analog. With regards to a ghrelin analong, nothing in the specification provides

guidance as to how to make and use a ghrelin analog. With regards to the use of any GHRH analog, while the specification indicates that other U.S. Patents have made or identified GHRH analogs, which improve its function as a GH secretagogue: decreased susceptibility to proteases, increased stability, and increased biological activity (specification, page 4, parag. 11), nothing in the specification provides guidance that expression of any of these GHRH analogs had activity like HV-GHRH, the analog used in the Examples, such that an artisan would predictably obtain piglets similar to the ones described in the Examples. For this reason, the specification does not enable the artisan to use the claimed invention for the full breadth of any analog. SEQ ID NO. 8 is an analog of growth hormone releasing hormone (HV-GHRH). No guidance was provided how to make and use analogs of this analog (e.g. see claim 5).

The claimed invention broadly encompasses any female mammal. The specification teaches the effects of GHRH and HV-GHRH on pigs (Example 20) and rats (Example 21). While the specification provides these two examples, the specification does not enable the claimed invention for its full breadth of any female mammal. While the specification provides guidance as to what the effects are of bovine GHRH (SEQ ID NO. 1) and HV-GHRH (SEQ ID NO. 8) on pigs and rats, the specification does not provide guidance as to what the effects are of GHRH and HV-GHRH and analogs of GHRH on other species of mammals. The art teaches not all mammals respond to heterologous proteins similarly. Hammer et al. (1986, J. Anim. Sci., 63: 269-278) teach transgenic mice expressing human growth hormone (hGH) show up to a fourfold enhancement in growth rate, while transgenic pigs expressing

hGH do not increase in weight gain (Hammer et al., page 276, 1st col. under "Effect of Foreign GH on Growth" to 2nd col.). Hammer et al.'s teaching indicates not all mammals predictably respond to expression of heterologous proteins and thus indicate that an artisan cannot predict whether any heterologous protein or analog of a protein would necessarily have activity in any host mammal. Thus, for this reason, the specification is limited to the embodiments taught: SEQ ID NO. 1 and SEQ ID NO. 8.

For these reasons, the specification does not provide guidance such that an artisan can practice the claimed invention for its full breadth.

Response to Arguments

Applicant's arguments, see pages 17-21 of Applicant's response, filed May 25, 2005, with respect to the rejection(s)of claim(s) 1, 5-13, 76, 80-88, 137, 138 under 35 U.S.C. 112, 1st parag. have been fully considered. Applicant's amendments have overcome some of the Examiner's rejections of February 25, 2005.

With regards to the issue of "in utero gene therapy" (Applicant's response, pages 18-19, under "in utero gene therapy"), while the Applicant indicates that the method claimed does not (Applicant's emphasis) introduce genetic material (nucleic acids) to the fetus directly or indirectly, the claims as written, encompass a method wherein the fetus could conceivably uptake plasmid DNA and thus be a subject of in utero gene therapy. It is noted, that claim 8, which encompasses a method of delivery includes a parenteral route, which includes administration via intravenously or intraperitoneally. Thus, the claims as written, encompass in utero gene therapy.

With regards to the issue of "gene therapy, Zanjani and Anderson" (Applicant's response, pages 19-20), Applicants have indicated that their amended claims overcomes several common problems of expression that were specifically addressed by Zanjani and Anderson. While Applicants have addressed the issues addressed by Zanjani and Anderson regarding unpredictability of gene therapy with regards to the independent claim, Applicants have not fully addressed the issues of unpredictability with regards to the dependent claims. It is noted, for example, that claim 8 encompasses the issue of enablement addressed by Zanjani and Anderson with regards to questions such as, "will the gene product be eliminated by the immune system or by some other mechanism?" and "are enough genes transferred into the cell?" as claim 8 encompasses administration of the vector via a parenteral route.

With regards to the issue of "gene therapy, Khan" (Applicant's response, page 20, the Applicants have indicated that the amended claims have overcome the problems of unpredictability in gene therapy taught by Khan. However, the Examiner disagrees. The issue at hand is that the art teaches that the effect of any transgene on any mammal is unpredictable. The Examiner has pointed out in the Office Action of February 25, 2005, that one of the problems with gene therapy is that an artisan cannot predict the effects (any phenotype(s) exhibited in any animal) of a heterologous protein expressed from a transgene. To clarify the matter, the Examiner has provided the discussion regarding Hammer et al., 1986's teaching above. While the claims broadly encompass growth hormones of SEQ ID NO. 1 and 8 and their analogs, no guidance

was given that SEQ ID NO. 1 and 8 and their analogs predictably have the same effects in all species of mammals.

With regards to the issue of Delivery Vectors, Stribley and Romano references, Applicant's response, page 20-21, Applicants' amendments to the claims have overcome the rejections.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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JH

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PRIMARY EXAMINER